
Non Toxic Goiter: Cytology, Histological Analysis: A Study in Mosul

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Abstract:

Objective: To determine the histological findings observed in non toxic goiter of the resected thyroid tissue in Mosul city & compare them with the results of Fine Needle Aspiration Cytology in order to assess the role of this method in the early diagnosis & correct management of both multinodular goiter & solitary thyroid nodule. Specimens were obtained from Al-Jumhuri Teaching Hospital & histological analysis was performed in the Department of Anatomy, College of Medicine, University of Mosul from January 2010 to June 2010.

Patients & Methods: Patients were classified according to the preoperative clinical diagnosis into those with non toxic multinodular goiter & those with solitary thyroid nodules, preoperative clinical diagnosis was confirmed by Fine Needle Aspiration Cytology in which patient lies supine with extended neck, the skin over the most prominent point of the goiterous thyroid is treated with antiseptics. A 10 ml syringe is used with a (21gauge) needle, gentle suction was applied & material was aspirated into the lumen of the syringe then the needle was disconnected & specimen was ejected onto a glass slide then smeared by sliding across another slide then fixed by spraying with fixative solution & examined & cytological reports of all the cases were prepared to be compared later with the histopathological reports of the removed thyroid tissue after operation. Postoperatively the biopsies were fixed in 10% formaline, processed & stained with Haematoxylline & Eosin for histological analysis. Statistical analysis of the histological findings was conducted using Chi-square test.

Results: non toxic goiter is more common in female than male. Fine needle aspiration cytology is a well established technique in the preoperative investigation of thyroid diseases. Specimens obtained from patients presented with multinodular goiter showed variable sized thyroid follicles, huge follicles were filled with colloid and lined by flattened epithelial cells; most of the nodules were not encapsulated. Specimens obtained from follicular adenoma showed well developed microfollicles with intact fibrous thin capsule. Degenerative changes in the stromal tissue such as haemorrhage, fibrosis & even calcification were present in some of the cases. Discrete thyroid swellings (solitary thyroid nodules) are present in 3–4% of the adult population; If hyperthyroidism associated with a discrete swelling it indicates a manifestation of toxic multinodular goiter. Solitary thyroid nodule was observed as a hard, irregular swelling with apparent unusual fixity associated with scanty normal follicular cells together with colloid.

Keywords: Goiter, Follicular adenoma, Solitary thyroid nodule.

Introduction:

Multinodular non toxic goiter is the most prevalent thyroid pathology worldwide characterized by unilateral or bilateral thyroid enlargement with morphologically and/or functionally transformed follicles and euthyroidism^[1]. Nodular goiter become a special health problem particularly in the endemic areas^[2]. Goiter is endemic when its prevalence is more than 10% in children aging between 6 to 12 years & sporadic when this prevalence is 10% or less^[3].

Deficiency in thyroid hormone production induced by iodine deficiency leads to increase TSH secretion resulting in hyperactive follicles with increased thyroid mass due to excessive cell replication & massive storage of colloid with or without nodularity called non toxic colloid goiter^[4].

Environmental factors such as malnutrition, drug, stress, pollution and infection and constitutional factors such as female gender, several genetic factors like circulating thyroid growth factors all contribute in different degree to the development of nodular thyroid enlargement^[5]. Smoking especially in the areas of mild iodine deficiency is associated with thyroid enlargement & goiter^[6] the use of oral contraceptives may reduce the risk of goiter^[7].

Thyroid nodule represents a significant diagnostic dilemma for the treating surgeon; it presents as discrete swelling in an otherwise impalpable gland which is considered as solitary

thyroid nodule or as dominant nodule in a clinically multinodular gland of a multinodular goiter^[8].

Five percent of thyroid nodules are malignant^[9], the prevalence is higher in children, in patient under age of 30 years and over age of 60 years & in those with history of radiation^[10]. On the other hand, malignancy rates are lower in multinodular goiter and predominantly in cystic lesion^[11]. However the exact cause of thyroid carcinoma is not well known but head and neck irradiation in childhood is a known predisposing factor^[12]. Moreover iodine deficient areas are known to have a high frequency of thyroid carcinoma^[1].

Fine needle aspiration cytology is a well established technique in the preoperative investigations of thyroid diseases, the technique is efficient, noninvasive, cost- effective, most sensitive & specific method in the diagnosis of solitary thyroid nodule^[13], it is the most commonly utilized procedure for obtaining thyroid tissue for cytological evaluation, it has been established as a safe and reasonably efficacious technique^[14].

Our study aimed to demonstrate the histological findings of both multinodular goiter & solitary thyroid nodule observed in the resected thyroid tissue & compare them with the results of Fine Needle Aspiration Cytology in order to assess the role of this method in the early diagnosis & correct management. FNA is performed with or without local lidocaine anesthesia by repetitively moving through the nodule a 21- to 27-gauge needle (most

frequently 25-gauge) attached to a 10-mL syringe; the syringe may be contained in a holder designed to facilitate the application of constant or intermittent suction. The aspirated material is smeared directly on slides, fixed, stained, and interpreted by cytopathologists^[15]. This technique is done by endocrinologists, cytopathologists, and surgeons, in the following conditions^[16]:

- ▶ Levels of thyroid stimulating hormone (TSH) should be measured and should be normal or elevated prior to aspiration,
- ▶ It is acceptable to perform FNA of all clinically palpable nodules typically ≥ 1 cm diameter particularly if ultrasound is limited.
- ▶ Ultrasound is strongly suggested either before or in conjunction with the FNA to identify those nodules meeting echographic criteria for the procedure.
- ▶ A family history or clinical factors that increase the likelihood of malignancy should be considered in the decision to aspirate even in the absence of the above indications.

Patients, Materials and Methods :

In this study 60 specimen of thyroid tissue were collected in Al-Jumhuri Teaching Hospital from sixty patients of both sexes who were admitted to the surgical out-patients department for the complaint of enlarged thyroid gland. Detailed history, thorough physical examination and hormonal assay (T3, T4 & TSH) were carried out, the history includes their age, sex, occupation, presence of pressure symptoms (like voice changes, dysphagia, stridor & choking sensation) in addition to drug history, family history of goiter & history of iodine deficiency & radiation during childhood. Patients were classified according to the preoperative clinical diagnosis into those with non toxic multinodular goiter & those with solitary thyroid nodule, preoperative clinical diagnosis was later confirmed by Fine Needle Aspiration Cytology and histopathological reports of the resected specimens.

All the patients showing multinodular goiter or thyroid nodules whether solitary or dominant nodule of multinodular who were decided to be operated on by surgeon were underwent FNAC which was done one day before operation.

Subtotal thyroidectomy was performed for those with multinodular goiter and lobectomy with isthmusectomy was performed for those with solitary thyroid nodule. Following the resection of thyroid tissue, the specimens were put in a fixative solution (10% neutral formalin) for 24 hour then each specimen was cut into 1 cm thick slices and dehydrated in graded alcohol solutions (70% alcohol for overnight, two changes in 90% alcohol one hour for each and two changes in 100% alcohol for two hours) then the specimens were immersed in xylene using three changes with one-hour interval for each. Complete removal of the clearing solution was made by immersing the tissue specimens into three successive paraffin bathes in oven, one hour for each. Finally paraffin blocks were prepared by embedding the tissue specimens using paraffin wax (melting point is 55-60°C) and these paraffin blocks were now ready for sections using Reichert Rotary Microtome, serial paraffin sections of 4 micrometers in thickness were cut from each block, the sections were collected and mounted (using DPX) on glass slides then the sections were stained with Haematoxylin and Eosin for histological analysis, we investigate & compare the size of thyroid follicles, presence of capsule and degenerative changes in both multinodular goiter and solitary thyroid nodule cases.

Results and Observations:

In this study the total number of cases included was 60, the ages of patients ranged from 10 to 70 years, 8 patients were male and 52 patients were female. The age and gender distribution is shown in Table I. We observed that the overall incidence of goiter in Mosul city in both sexes increase between 20 to 50 years & it affect female more than male.

Table I : Age & sex distribution in 60 patients presented with goiter included in the study.

Age (years)	Male	Female	Total	%
10-20	1	7	8	13.3
21-30	3	17	20	33.3
31-40	1	11	12	20
41-50	2	12	14	23.3
51-60	0	3	3	5
61-70	1	2	3	5

- Among the sixty cases included in the study correlation of FNAC findings and histopathological reports of operated patients was shown in Table II:

➤ FNAC diagnosed 52 (86.66%) cases as benign and 8 (13.32%) as malignant as shown in Table II :30 cases (50%) were reported as non toxic multinodular goiter.11(18.33%)cases as follicular tumour, but it can not differentiate whether they were benign or malignant tumour according to presence or absence of capsular or vascular invasion. 8(13.33%) cases as subacute thyroiditis and 3(5%) cases as Hashimoto's thyroiditis. In the malignant group of 10 cases 2(3.33%) were reported as follicular carcinoma, 5(8.33%) as papillary carcinoma, 1(1.66%) as undifferentiated carcinoma and 2(3.33%) as lymphoma.

➤ Histopathological findings observed in the patient's reports diagnosed 54 (81.66%) benign

lesions and 6(18.33%) as malignant lesions as shown in Table II: 29 cases (48.33%) were reported as non toxic multinodular goiter, 14(23.33%) reported as follicular tumours of which 5(8.33%) cases as follicular adenoma which revealed no capsular or vascular invasion & 9 (15%) cases as follicular carcinoma in which vascular & capsular invasion was obvious, 7(11.6%) as subacute thyroiditis and 4(6.66%)cases as Hashimoto's thyroiditis. In the malignant group of 6 (9.88%) cases, 4(6.66%) as papillary carcinoma, 1(1.66%) as undifferentiated carcinoma and 1(1.66%) as lymphoma.

Table II : Analytic comparison of FNAC with histopathological results of thyroid tissue biopsies from 60 patients presented with goiter.

Diagnosis	Histopathological Diagnosis	FNAC findings
Benign	54 (81.66%)	52 (86.66%)
<i>Nontoxic multinodular goiter</i>	29 (48.33%)	30 (50%)
<i>Follicular tumour</i>	14(23.33%)	11(18.33%)
<i>Follicular adenoma</i>	5(8.33%)	Cannot differentiate
<i>Follicular carcinoma</i>	9 (15%)	
<i>Subacute thyroiditis</i>	7(11.6%)	8(13.33%)
<i>Hashimoto's thyroiditis</i>	4(6.66%)	3(5%)
Malignant	6(9.98%)	8(13.32%)
<i>Papillary carcinoma</i>	4(6.66%)	5(8.33%)
<i>Undifferentiated carcinoma</i>	1(1.66%)	1(1.66%)

➤ **Histological findings:**

- Specimens obtained from patients presented with multinodular goiter showed variable sized thyroid follicles either microfollicles, medium sized follicles or large sized follicles (Fig.1), some nodules are composed of huge follicles, filled with colloid and lined by flattened epithelial cells, others were extremely cellular & hyperplastic, their colloid was pale and finely vacuolated, all the nodules were well circumscribed, most of them were not encapsulated (Fig. .2)
- Macrofollicular nodules may show areas of cystic degeneration with cellular debris & hemosiderin - laden macrophages (Fig. .3).
- Another benign thyroid disease associated with goiter is follicular adenoma showed well developed microfollicles with intact fibrous thin capsule, the architectural & histological appearance was different

from multinodular goiter and also from that of the surrounding normal tissue which showed signs of compression, there was no vascular or capsular invasion and considerably few colloid (Fig.4) The follicular cells are crowded and may form clusters.

- Degenerative changes in the stromal tissue such as hemorrhage (Fig.5), fibrosis & even calcification were present in some of the cases with variable number of chronic inflammatory cells indicating coexistence of chronic thyroiditis (Fig.6).

In this study, FNAC showed an accuracy of 96.6%, sensitivity of 75%, specificity of 95.83%, positive predictive value of 81.81% and negative predictive value of 93.81%. Comparison of histopathological findings with FNAC revealed two false positive results and three false negative results (Table III).

Table III : Correlation of FNAC & Histopathological Findings

Diagnosis	FNAC	Histopathological
False positive=2	Papillary carcinoma(1)	Nodular goiter
	Lymphoma(1)	Hashimoto's thyroiditis
False negative=3	Subacute thyroiditis(1)	Follicular carcinoma
	Nodular goiter (2)	Follicular carcinoma

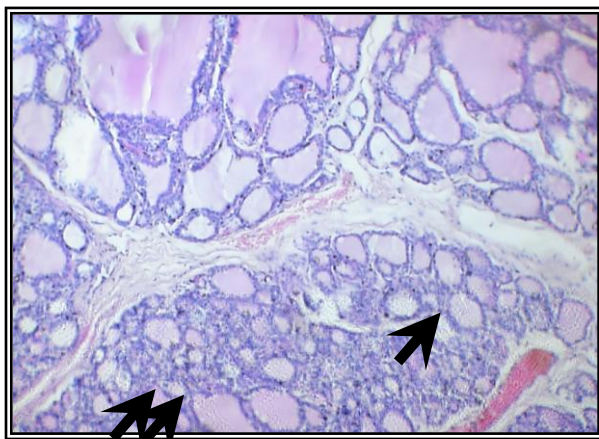


Fig.1: Photomicrograph of thyroid tissue from patient presented with multinodular goiter showed variable sized thyroid follicles either micofollicles (arrow), medium sized follicles (arrow), or large sized follicles (arrow) all the nodules were well circumscribed with no capsule (H&E X100).

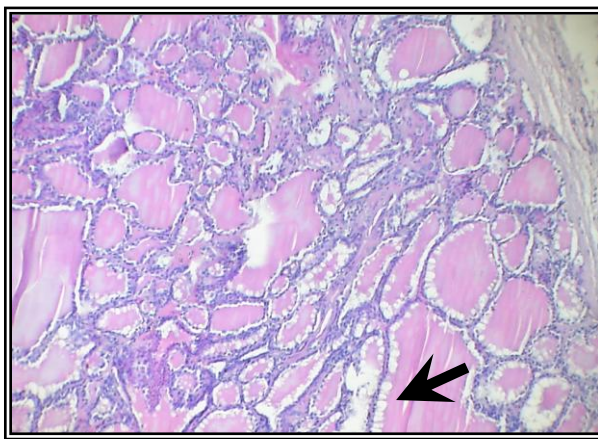


Fig.2: Photomicrograph of thyroid tissue from patient presented with multinodular goiter showed thyroid follicles filled with pale and finely vacuolated colloid and lined by flattened epithelial cells (H&E X100).

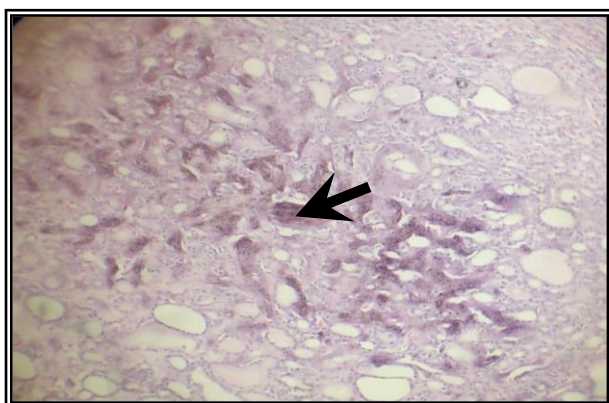


Fig.3: Photomicrograph of multinodular goiter showing areas of cystic degeneration with cellular debris & hemosiderin-laden macrophages (arrow) (Fig.2).

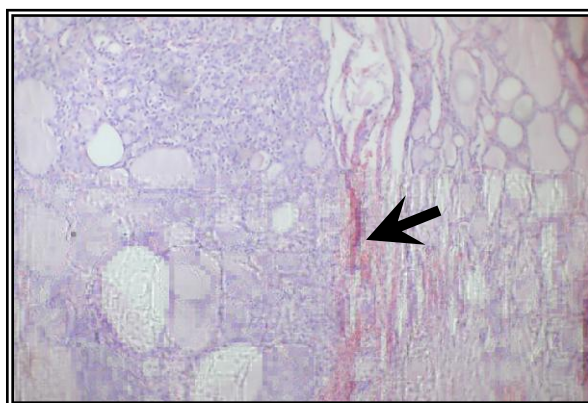


Fig.4: Photomicrograph of follicular adenoma (arrow) showing intact fibrous thin capsule (arrow) with compression of the surrounding normal tissue (arrow), no vascular or capsular invasion and considerably few colloid (H&E X100).

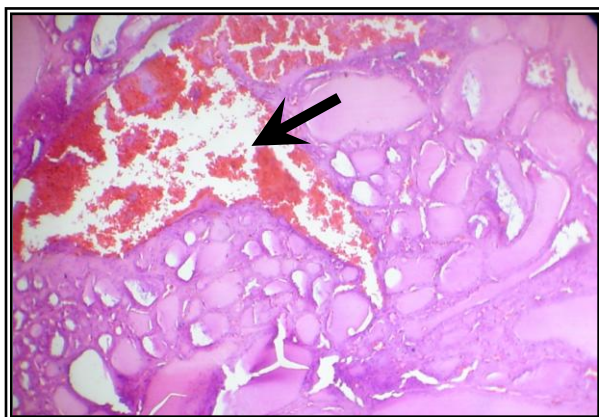


Fig.5: Photomicrograph of goiterous thyroid tissue showing haemorrhage in the stromal tissue (arrow) indicating coexistence of chronic inflammatory process (H&E X100).

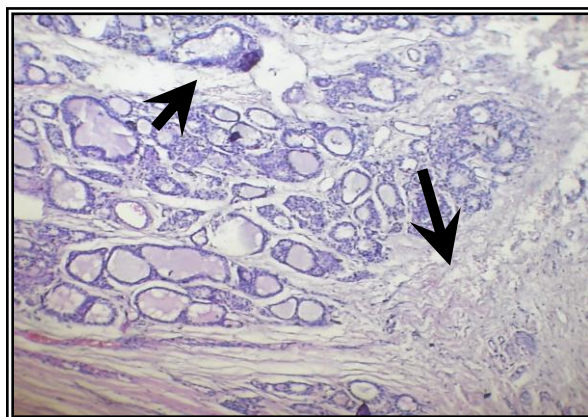


Fig.6: Photomicrograph of goiterous thyroid tissue showing fibrosis of the stromal tissue (arrow) with thickened trabeculae separating between the lobules (H&E X100).

Discussion:

Nontoxic goiter may be presented as diffuse or nodular enlargement of thyroid gland which is not associated with thyrotoxicosis and does not result from an autoimmune or inflammatory process. We found that goiter is more common in female than male and this agree with Saddique M. et.al, 2008^[8] who stated that multinodular goiter is more prevalent in female and more liable to malignancy than in male, in addition the incidence of thyroid cancer is more in patients between 20 and 60 years old. Kumar et.al, (2008)^[17] observed that goiter is predominantly a disease of women, the female to male ratio is about 2.5:1.

Our finding agree with the international figures of thyroid disease which stated that thyroid malignancy is predominant in the old aged female group^[185] In our study the incidence of thyroid cancer is 16.6% while a strikingly high incidence of surgically treated thyroid malignancy was reported in three studied from Al-Riyadh ranging from 21% to 29%^{[19] [20]}.

In our study undifferentiated carcinoma constitute 3.2% of the study group, similar percentage (<5%) was reported by Rossi RL. et.al, (2001)^[21]

It was assumed that simple multinodular goiter is unlikely to be malignant, the risk of malignancy is higher in a solitary thyroid nodule, thus a dominant nodule in a multinodular goiter as well as a single nodule should be evaluated^[22]. The present study showed an accuracy of 96.6%, sensitivity of 75%, specificity of 95.83%, Positive predictive value of 81.81% & Negative predictive value of 93.81%, which is similar to Nggada HA & Khalil MI, (2003)^[23] revealed an accuracy of 94.2%, sensitivity of 88.9% and specificity of 96.1% and suggested that FNAC is more specific than sensitive in detecting thyroid diseases. this result agree with Nasuti J. et.al, (2002)^[24] who reported that FNAC is highly accurate, specific & sensitive technique which play a significant role in the diagnosis & management planning of multinodular goiter & solitary thyroid nodules, it is cost-effective and free of complication in expert hands.

We observed that surgical specimens of non toxic multinodular goiter contains irregularly enlarged thyroid follicles lined by flattened epithelium filled with colloid material containing clear vacuoles due to increased activity of the epithelium to produce more thyroid hormone this finding agree with that of Hermus AD 2002^[25].

Microfollicles may be seen in smears obtained from follicular adenoma, they do not show vascular or capsular invasion this observation similar to Oertel YC, (2002)^[26].

Conclusion:

Incidence of multinodular goiter in Mosul city is more in female than male & in both sexes it increases between 20 to 50 years of age. Fine Needle Aspiration Cytology is highly accurate, specific & sensitive technique which play a significant role in the diagnosis & management planning of multinodular goiter & solitary thyroid nodules.

Recommendation:

- ▶ We recommend other workers in future to study the ultrastructural changes of thyroid tissue in multinodular goiter and in solitary thyroid nodule in Mosul.
- ▶ A research to study thyroid biopsies collected by Trucut needle and compare the observed findings with the histopathological findings of the resected thyroid tissue.
- ▶ A work to investigate the cytological and histological changes of thyroid cancer.

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